

Case Report: Cutaneous Leishmaniasis in Cuban Immigrants to Texas who Traveled through the Darién Jungle, Panama

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Abstract. Cutaneous leishmaniasis is rarely seen in the United States. Four Cuban immigrants traveled along the same route at different times from Cuba to Ecuador, then northward, including through the Darién Jungle in Panama. These patients had chronic ulcerative non-healing skin lesions and were given a diagnosis of leishmaniasis.

Leishmaniasis is a vector-borne disease caused by the protozoan parasite of the genus *Leishmania* and is spread by the bite of sand flies from the sub-family *Phlebotominae*.¹ There are various clinical manifestations of leishmaniasis, including cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis, and visceral leishmaniasis. Cutaneous leishmaniasis occurs at the site of the bite, with lesions forming weeks to months later starting with a papule, which then develops into a nodule or plaque-like lesion and progresses to a painless ulceration with an indurated border.

We report four cases of CL caused by *Leishmania (Viannia) panamensis* in Cuban immigrants who traveled through the Darién Gap Jungle between Colombia and Panama on their journey north to the United States. This region has been shown to have high transmission rates of leishmaniasis,² and, in 2012, Panama experienced an outbreak beyond expected endemic rates.³ This case series highlights a previously underappreciated immigration route to the United States for Cubans and the need to include leishmaniasis as a differential diagnosis for non-healing skin ulcers in this patient population.

During May 2012–April 2013, four persons who had recently immigrated to the United States from Cuba came to the National School of Tropical Medicine at Baylor College of Medicine's (BCM) Tropical Medicine Clinic for non-healing skin ulcers. All four persons reported a similar route of travel from Cuba to Texas (Figure 1), although at different times. Each person began their journey by flying to Quito, Ecuador, where they then traveled by bus through Colombia, passing through the cities of Pasto and Cali to Quibdó. In Quibdó, they took a short flight to Bahía Solano, Colombia, where a boat ride then transported them to Punta Ardita near the Panama border. They then traveled by foot through the thick jungle in Darién, Panama, for 5–15 days. During this time, they slept outdoors and reported numerous insect bites. Once through the Darién area, they traveled northward until they entered the United States at the Mexican border.

Once in the United States, the four persons sought medical care at outside clinics for skin lesions that had developed within two months after they passed through the Darién. They were treated for presumed infection with *Staphylococcus aureus*. The antibiotics had no therapeutic effect, and the

lesions continued to grow and develop into non-healing, painless ulcers with accompanying satellite lesions. Once in Houston, Texas, the four persons were directed to the Department of Dermatology at BCM (Table 1).

Patient 1 was a 38-year old woman with a three-month history of an expanding, painless, pruritic ulcer who had a 5-cm ulcer on her proximal right arm, along with several satellite lesions covered with crusts, as well as a 1.5-cm erythematous papule with central ulceration covered in crust on her right thigh. Patient 2 was a 46-year old man who had a two-month history of two erythematous, scaly plaques with central ulceration on the left forearm (Figure 2A). Patient 3 was a 43-year old man with a two-month history of non-healing, tender lesions that on presentation were a 5-cm crusted nodule at the vertex of the patient's scalp and two right parietal 1 cm papules, as well as a fluctuant nodule on his right lower leg. Patient 4 was a 43-year old woman who had a two-month history of a slowly expanding, painless lesion on her cheek, which on examination was a 1.5-cm eroded nodule on her left malar area and four papules above the main lesion (Figure 2C). All of the patients reported the lesions appearing from two weeks to two months after traveling through the Darién area. No lesions were noted before traveling through this region. The patients all denied systemic complaints including fevers, chills, night sweats, and weight loss, and were otherwise normal on physical exam. No mucosal involvement was noted in any of the patients upon exam.

For each of the patients, a punch biopsy was performed by the Department of Dermatology for diagnosis by histologic analysis by BCM, and species-specific polymerase chain reaction and culture performed by the Centers for Disease Control and Prevention (Atlanta, GA). All biopsy specimens showed dense inflammatory infiltrates in the dermis with numerous histiocytes, lymphocytes, and intracellular structures within macrophages. These structures were identified as small organisms with kinetoplasts suggestive of *Leishmania* amastigotes. Numerous dermal plasma cells were also seen in biopsy specimens from patients 1, 2, and 4. Biopsy specimens from patient 3 showed dermal multinucleated giant cells, and scattered dermal eosinophils were observed in biopsy specimens from patient 4. Using polymerase chain reaction, PCR, CDC identified *L. (V.) panamensis*, a parasitic infection found in Belize, Colombia, Costa Rica, Ecuador, Honduras, Nicaragua, Panama, and Venezuela.⁴

All the patients were treated with liposomal amphotericin B (AmBisome), 3 mg/kg/day for 5 days, followed by two infusions

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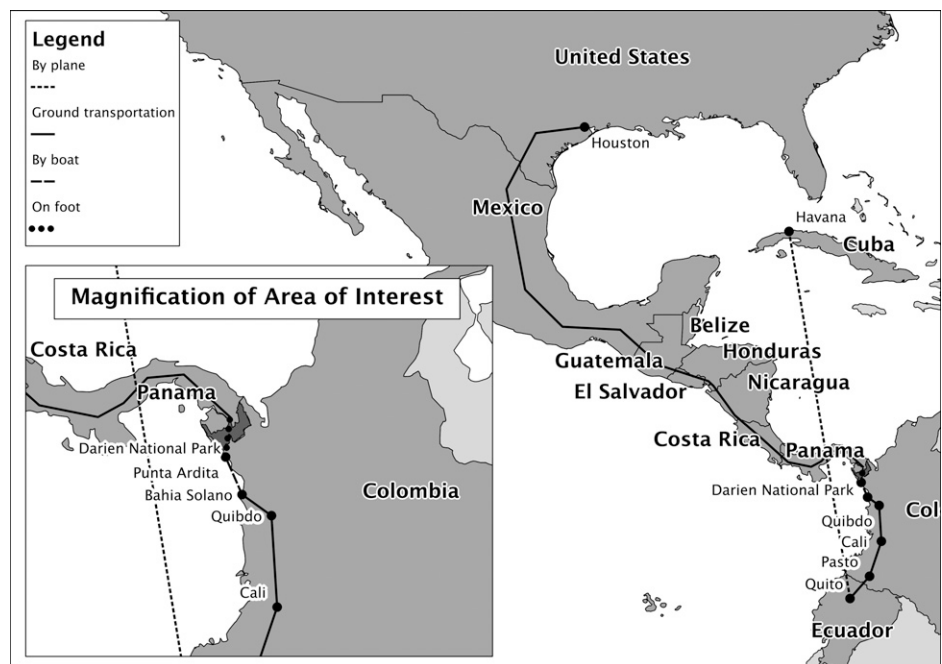


FIGURE 1. Map showing immigration route of a cluster of Cuban patients with cutaneous leishmaniasis caused by *Leishmania (V.) panamensis*. Note the travel by foot through the thick jungle of the Darién National Park, Panama, where they likely contracted the disease.

at the same dose on days 14 and 21 to complete a total treatment of 21 mg/kg,⁵ a dosing found to be effective in treating CL.⁶ In an attempt to minimize infusion-related reactions, the patients were pre-treated with 50 mg of diphenhydramine and 650 mg of acetaminophen, and hydrated with 500 mL of normal saline before each infusion.⁶ Despite this treatment, patient 1 experienced a mild self-resolving infusion-related reaction with chills and a headache. Three patients experienced an elevation of the creatinine level (two times the reference value) that resolved within days.

Patients were followed-up by the Tropical Medicine Clinic over several months because healing of these ulcers is slow. Patients 1 and 4 had good resolution (Figure 2D), and patient 2 had a small, 1-cm, dry, scabbed lesion at five months post-treatment. Concern over incomplete resolution led to a 30 day course of itraconazole, 200 mg twice a day, which led to good resolution of the lesion and a leishmaniasis-negative biopsy result (Figure 2B). Patient 3 had the most extensive disease, with 13 lesions upon presentation, and during his treatment with liposomal amphotericin B, continued to have disease progression. Concern for treatment failure led to additional therapy with intravenous sodium stibogluconate (pentostam),

starting at 50% of the dose (10 mg/kg/day), and increasing to 75% (15 mg/kg/day) on day 5, then 100% (20 mg/kg/day) on day 10 to complete a total of 20 days of therapy, as recommended by the Parasitic Diseases Branch of CDC (personal communication). Currently, his lesions are resolving well.

Liposomal amphotericin B was chosen because all patients had extensive disease, and in the case of patient 4, the lesion was on her face, where scarring is undesirable. Liposomal amphotericin B therapy for CL has been shown clinically to be effective, with improved lesion resolution and less toxicity than sodium stibogluconate.^{1,6–12} Treatment not only promotes healing of the cutaneous lesion, but also reduces the risk of subsequent mucosal involvement.^{13,14} Up to 12% of CL cases are at risk of later developing mucocutaneous leishmaniasis, depending on the subspecies of *Leishmania Viannia*; either *braziliensis* or *guyanensis* have the highest risk.¹⁵ Mucocutaneous leishmaniasis presents as cutaneous lesions in addition to mucosal destruction, most commonly of the nose, mouth, or nasal septum. Mucosal destruction can be disfiguring and may occur years after the development of cutaneous lesions.

This report highlights a previously underappreciated immigration route for Cubans through Central America, which

TABLE 1

Patient demographics, disease presentation, and treatment course of four Cuban immigrants who came to the National School of Tropical Medicine at Baylor College of Medicine's Tropical Medicine Clinic in Houston, TX for non-healing skin ulcers, May 2012–April 2013*

Patient	Age, years/sex	Lesion location; size; presence of satellite lesions (+/-)	Diagnosis and pathogen	Duration of disease before initiation of treatment	Treatment course
1	38/F	Proximal right posterior arm; 5 cm; (+)	CL <i>L. (V.) panamensis</i>	3 months	AmBisome (days 1–5, 14, 21)
2	46/M	Distal left forearm; 2 lesions: 4 cm and 3 cm; (+)	CL <i>L. (V.) panamensis</i>	2 months	AmBisome (days 1–5, 14, 21); then itraconazole (daily, 30 days)
3	43/M	Vertex of scalp, 8 more lesions on eyes, legs, and torso; 5 cm, other lesions 1 cm; (+)	CL <i>L. (V.) panamensis</i>	2 weeks	AmBisome (days 1–5); then pentostam (daily, 20 days)
4	43/F	Left malar area; 1.5 cm; (+)	CL <i>L. (V.) panamensis</i>	3 months	AmBisome (days 1–5, 14)

* CL = cutaneous leishmaniasis.

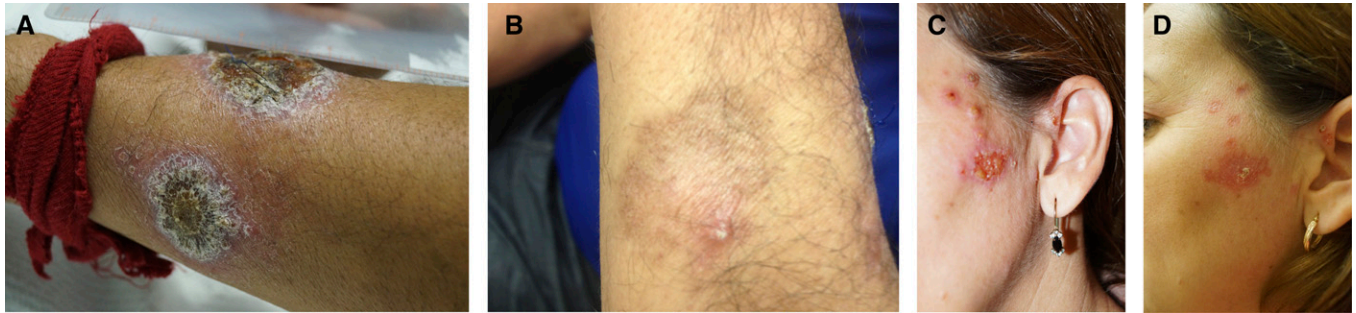


FIGURE 2. Skin ulcers of two of the four Cuban immigrants to the United States with cutaneous leishmaniasis caused by *Leishmania* (*V.*) *panamensis*. **A**, Patient 2, showing two erythematous, scaly plaques with central ulceration and diameters of 3 cm and 4 cm on the left forearm. **B**, Patient 2 at six months post-treatment showing good resolution of the lesions. **C**, Patient 4, showing a 1.5-cm eroded nodule on left malar area and four papules above the main lesion. **D**, Patient 4 at three months post treatment showing with good resolution of the lesions.

places immigrants at risk for a number of emerging tropical diseases, including leishmaniasis. Physicians should be aware of this immigration route when treating Cuban immigrants and include leishmaniasis in the differential diagnosis when treating non-healing skin ulcers in this patient population. Liposomal amphotericin B can be a well-tolerated and efficacious treatment of CL caused by *L. (V.) panamensis*.

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